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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: MRP3 GENES AND USES THEREOF

(57) Abstract: A nucleic acid capable of driving the expression of a reporter gene in a cancer cell line is disclosed. A polypeptide able to confer multidrug-resistance on a cell is disclosed. Also disclosed are nucleic acids encoding the polypeptide, expression vectors, transformant host cell lines expressing the polypeptide, and antibodies binding to the polypeptide. Screening, diagnostic and treatment methods using the above polypeptide, nucleic acids, antibodies and host cell lines are also within the scope of this invention.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/05335

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C07K 13/00; C07H 21/04
US CL : 530/350; 536/22.1; 435/252.3, 325
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 530/350; 536/22.1; 435/252.3, 325

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DUSSAULT et al. Peptide Mimetic HIV Protease Inhibitors Are ligands for the Orphan Receptor SXR. The Journal of Biological Chemisry. 2001, Vol. 276, No. 36, pages 33309-33312.	1-12 and 24
A	HAU et al. Pegylated Liposomal Doxorubicin-Efficacy in Patients with Recurrent High-Grade Glioma. Cancer. 2004, Vol. 100, No. 6, pages 1199-1207.	1-12 and 24

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
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INTERNATIONAL SEARCH REPORT

International application No.
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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
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BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-12 and 24, drawn to an isolated nucleic acid comprising a nucleotide sequence which is at least 70% identical to the sequence of SEQ ID NO: 3 encoding with the amino acid sequence of SEQ ID NO: 2 and method of producing a polypeptide by using the sequence.

Group II, claim(s) 13-16, drawn to a nucleic acid sequence further comprising SEQ ID NO: 1.

Group III, claim(s) 17-18, drawn to an isolated polypeptide comprising an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID NO: 2.

Group IV, claim(s) 19-22, drawn to an expression vector comprising a first nucleic acid sequence comprising SEQ ID NO: 3 and a second nucleic acid sequence encoding a gene.

Group V, claim(s) 23, drawn to a purified antibody.

Group VI, claim(s) 25-30, drawn to a method for detecting a cellular proliferative disorder in a subject via measuring the level of a gene encoding a polypeptide with sequence of SEQ ID NO 2.

Group VII, claim(s) 31-33, drawn to a method for monitoring a subject undergoing a therapeutic treatment.

Group VIII, claim(s) 34, drawn to a method for targeting a cellular proliferative disorder in a subject.

Group IX, claim(s) 35, drawn to a method for expression a foreign polypeptide in a cell in vivo.

Group X, claim(s) 36, drawn to a method for introducing a foreign nucleic acid into a cell in vivo.

Group XI, claim(s) 37 drawn to a method for targeting a cellular proliferative disorder in a subject via administering to the subject an agent that can bind to a nucleic acid comprising the nucleotide of SEQ ID NO: 3,

Group XII, claim(s) 38, drawn to a method for targeting a cellular proliferative disorder in a subject via administering to the subject an agent that can modulate the expression level of a gene encoding to a polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

Group XIII, claim(s) 39, drawn to a method for modulating the cellular pump mechanism of a resistant tumor cell.

Group XIV, claim(s) 40, drawn to a metlhod for modulating the cellular pump mechanism of a resistant tumor cell via administering to a subject having a resistant tumor cell an agent that binds to a polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

Group XV, claim(s) 41-43, drawn to a method for screening for a therapeutic agent for treating a drug-resistant tumor cell.

Group XVI, claim(s) 44-46, drawn to a cell for screening for a therapeutic agent for treating a drug-resistant tumor cell.

Group XVII, claim(s) 47, drawn to a method for making an antibody by immunizing a non-human animal with an immunogenic fragment of a polypeptide with the sequence of SEQ ID NO: 2.

Group XVIII, claim(s) 48, drawn to a method for making an antibody comprising providing a hybridoma cell.

Group XIX, claim(s) 49, drawn to a method for modulating expression of a gene responsible for controlling cellular pump mechanisms in cell.

Group XX, claim(s) 50, drawn to a method for delivering a suicide protein to a tumor cell.

The inventions listed as Groups I-XX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The Products groups I-V and XVI claim different products, for example, Groups I and II are drawn to nucleic acid, Group III is drawn to polypeptide, Group IV is drawn to an expression vector which comprises different sequences from the nucleic acid sequence claimed in Groups I and II. Group V is drawn to antibody, and Group XIV is drawn to a cell for screening for a therapeutic agent. Because of the different molecular structures of the products, thus, they are different invention.

Among Groups I and II, Group I is drawn to an isolated nucleic acid comprising a nucleotide sequence which is at least 70% identical to the sequence of SEQ ID NO: 3, while Group II is drawn to a nucleic acid sequence further comprising SEQ ID NO: 1.

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The method Groups VI-XV and XVII-XX are drawn to different methods as set forth in their preambles and the different method steps. Thus they lack the same or corresponding special technical features.

Continuation of B. FIELDS SEARCHED Item 3:
WEST AND STN SEARCHED; MEDLINE, CAPLUS, BIOSIS, EMBASE.
search terms: SEQ ID NO: 3 and 2, producing polypeptide, expression vector